



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Peng Cho TANG et al.

Title: TRICYCLIC QUINOXALINE DERIVATIVES AS PROTEIN TYROSINE KINASE INHIBITORS

Appl. No.: 10/714,399

Filing Date: 11/17/2003

Examiner: Unassigned

Art Unit: Unassigned

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

The USPTO has waived the requirement under 37 CFR 1.98(a)(2)(i) to submit copies of U.S. patents and U.S. patent application publications when citing and submitting an Information Disclosure Statements in a patent application filed after June 30, 2003 and in an international application that has entered the national stage under 37 USC §371 after June 30, 2003. Accordingly, copies of these types of documents are not being supplied in connection with this application. Reference is being made to Final OG Notice from Office of Patent Legal Administration dated August 5, 2003, *Information Disclosure Statements May Be Filed Without Copies of U.S. Patents and Published Applications in Patent Applications filed after June 30, 2003.*

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in parent application Serial No. 09/948,090, filed 09/07/2001, now U.S. Patent No. 6,656,940, which is a divisional of application Serial No. 09/129,139, filed August 4, 1998, now U.S. Patent No. 6,329,375. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent applications.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

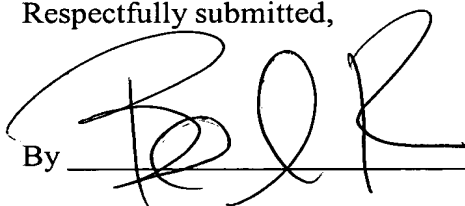
Applicants respectfully request that the listed documents be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date April 16, 2004

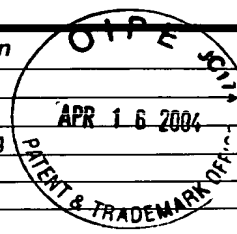
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By 

Beth A. Burrous  
Attorney for Applicant  
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Substitute for form 1449B/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				<b>Complete if Known</b>	
Sheet		1	of	6	Application Number 10/714,399 Filing Date 11/17/2003 First Named Inventor Peng Cho Tang Group Art Unit Unassigned Examiner Name Unassigned Attorney Docket Number 034536-0893



U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	A1	4,966,849	A	VALLEE et al.	10-30-1990	
	A2	5,116,843	A	MERTENS et al.	05-26-1992	
	A3	5,217,999	A	LEVITZKI et al.	06-08-1993	
	A4	5,302,606	A	SPADA et al.	04-12-1994	
	A5	5,330,992	A	EISSENSTAT et al.	07-19-1994	
	A6	5,476,851	A	MYERS et al.	12-19-1995	
	A7	5,932,580	A	LEVITZKI et al.	08-03-1999	

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
X	A8	WO	94/10202	A1	GENENTECH, INC.	05-11-1994		
X	A9	WO	94/03427	A1	WARNER-LAMBERT COMPANY	02-17-1994		
X	A10	WO	92/21660	A1	PFIZER, INC.	12-10-1992		
X	A11	WO	91/15495	A1	PFIZER, INC.	10-17-1991		
X	A12	WO	94/14808	A1	FARMITALIA CARLO ERBA SRL	07-07-1994		
X	A13	WO	92/20642	A1	RHONE-POULENC RORER INTERNATIONAL	11-26-1992		
X	A14	EP	0 566 226	A1	ZENECA LIMITED	11-08-1995		

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✓	A15	ABDEL-MAGEID et al., STN International® CAPLUS Database, Accession No. 1981:30703, <u>Egypt J. Chem.</u> , 20(5), 427-439, (1980)	
✓	A16	ACHIWA et al., "Sunthesis and mutagenicity of a new mutagen, 2-amino-1,7,9-trimethylimidaza-[4,5-g] quinoxaline, and its analog," <u>Chem. Pharm. Bull.</u> 42:408-409 (1994)	
✓	A17	AKBASAK and SUNAR-AKBASAK et al., "Oncogenes: cause or consequence in the development of glial tumors," <u>J. Neurol. Sci.</u> , 111:119-133 (1992)	
✓	A18	ANDREANI et al., "Synthesis and potential coanthracyclic activity of substituted 3-(5-imidazo[2,1-b] thiazolymethylene)-2-indolinones," <u>Eur. J. Med. Chem.</u> , 32:919-924 (1997)	
✓	A19	ARTEAGA et al., "Blockade of the Type I Somatomedin Receptor Inhibits Growth of Human Breast Cancer Cells in Athymic Mice," <u>J. Clin. Invest.</u> , 84:1418-1423 (1989)	
✓	A20	BASERGA, "The Insulin-like Growth Factor I Receptor: A Key to Tumor Growth?" <u>Cancer Research</u> 55:249-252 (1995)	
✓	A21	BASERGA, "Oncogenes and the Strategy of Growth Factors," <u>Cell</u> , 79:927-930 (1994)	
✓	A22	BOLEN et al., "Nonreceptor tyrosine protein kinases," <u>Oncogene</u> 8:2025-2031 (1993)	
✓	A23	BOLEN et al., "The Src family of tyrosine protein kinases in hemopoietic signal transduction," <u>FASEB J.</u> 6:3403-3409 (1992)	
✓	A24	BONNER et al., "Structure and Biological Activity of Human Homologs of the raf/mil Oncogene," <u>Molecular and Cellular Biology</u> 5:1400-1407 (1985)	
✓	A25	COPPOLA et al., "A Functional Insulin-Like Growth Factor I Receptor is Required for the Mitogenic and Transforming Activities of the Epidermal Growth Factor Receptor," <u>Molecular and Cellular Biology</u> 14:4588-4595 (1994)	

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		<b>Examiner Name</b>	Unassigned
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Sheet	3	of	6

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X	A26	DECKER and LOHMANN-MATTHES, "A quick and simple method for the quantitation of lactate dehydrogenase release in measurements of cellular cytotoxicity and tumor necrosis factor (TNF) activity," <u>J. Immunol. Methods</u> 15:61-69 (1988)	
X	A27	DICKSON et al., "Tyrosine kinase receptor-nuclear protooncogene interactions in breast cancer," <u>Cancer Treatment Res.</u> 61:249-273 (1992)	
X	A28	FANTL et al., "Distinct Phosphotyrosines on a Growth Factor Receptor Bind to Specific Molecules That Mediate Different Signaling Pathways," <u>Cell</u> 69:413-423 (1992)	
X	A29	FENDLY et al., "Characterization of Murine Monoclonal Antibodies Reactive to Either the Human Epidermal Growth Factor Receptor or HER2/neu Gene Product," <u>Cancer Research</u> 50:1550-1558 (1990)	
X	A30	FINGL and WOODBURY, "Chapter 1 - General Principles," in <u>The Pharmacological Basis of Therapeutics</u> 5th edition, Goodman and Gilman editors, MacMillan Publishing Co., Inc., New York, pp. 1-46 (1975) © MacMillan Publishing Co. Inc.	
X	A31	FLOEGE et al., "Factors involved in the regulation of mesangial cell proliferation <i>in vitro</i> and <i>in vivo</i> ," <u>Kidney International</u> 43:S47-S54 (1993) © International Society of Nephrology	
X	A32	FRIDMAN et al., "Derivatives of imidazobenzothiadiazole, imidazobenzoselenodiazole, imidazobenzotriazole and imidazoquinoline," <u>J. Gen. Chem. USSR</u> 32:2829-2838 (1962)	
X	A33	GOLDRING and GOLDRING, "Cytokines and Cell Growth Control," <u>Critical Reviews in Eukaryotic Gene Expression</u> 1:301-326 (1991)	
X	A34	HONEGGER et al., "Point Mutation at the ATP Binding Site of EGF Receptor Abolishes Protein-Tyrosine Kinase Activity and Alters Cellular Routing," <u>Cell</u> 51:199-209 (1987) © Cell Press	
X	A35	JELLINEK et al., "Inhibition of Receptor Binding by High-Affinity RNA Ligands to Vascular Endothelial Growth Factor," <u>Biochemistry</u> 33:10450-10456 (1994) © American Chemical Society	
X	A36	KENDALL and THOMAS, "Inhibition of vascular endothelial cell growth factor activity by an endogenously encoded soluble receptor," <u>Proc. Natl. Acad. Sci. USA</u> 90:10705-10709 (1993)	

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X	A37	KIM et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth in vivo," <u>Nature</u> 362:841-844 (1993)	
X	A38	KINSELLA et al., "Protein Kinase C Regulates Endothelial Cell Tube Formation on Basement Membrane Matrix, Matrigel," <u>Exp. Cell Research</u> 199:56-62 (1992) © Academic Press, Inc.	
X	A39	KOCH et al., "SH2 and SH3 Domains: Elements That Control Interactions of Cytoplasmic Signaling Proteins," <u>Science</u> 252:668-674 (1991)	
X	A40	KOMADA and KITAMURA, "The cell dissociation and motility triggered by scatter factor/hepatocyte growth factor are mediated through the cytoplasmic domain of the c-Met receptor," <u>Oncogene</u> 8:2381-2390 (1993)	
X	A41	KORC et al., "Overexpression of the Epidermal Growth Factor Receptor in Human Pancreatic Cancer Is Associated with Concomitant Increases in the Levels of Epidermal Growth Factor and Transforming Growth Factor Alpha," <u>J. Clin. Invest.</u> 90:1352-1360 (1992) copyright The American Society for Clinical Investigation, Inc.	
X	A42	KORZENIEWSKI and CALLEWAERT, "An Enzyme-Release Assay for Natural Cytotoxicity," <u>J. Immunol. Methods</u> 64:313-320 (1983) © Elsevier Science Publishers	
X	A43	KUMABE et al., "Amplification of $\alpha$ -platelet-derived growth factor receptor gene lacking an exon coding for a portion of the extracellular region in a primary brain tumor of glial origin," <u>Oncogene</u> 7:627-633 (1992)	
X	A44	LEE and DONOGHUE, "Intracellular Retention of Membrane-Anchored v-sis Protein Abrogates Autocrine Signal T transduction," <u>J. Cell. Biol.</u> 118:1057-1070 (1992) © The Rockefeller University Press	
X	A45	MACAULAY et al., "Autocrine Function for Insulin-like Growth Factor I in Human Small Cell Lung Cancer Cell Lines and Fresh Tumor Cells," <u>Cancer Research</u> 50:2511-2517 (1990)	
X	A46	MARIANI et al., "Inhibition of angiogenesis by FCE 26806, a potent tyrosine kinase inhibitor," <u>Experimental Therapeutics - Proceedings of the American Association for Cancer Research</u> 35:381 at abstract no. 2268 (March 1994)	
L	A47	MORRISON et al., "Signal Transduction From Membrane to Cytoplasm: Growth Factors and Membrane-Bound Oncogene Products Increase Raf-1 Phosphorylation and Associated Protein Kinase Activity," <u>Proc. Natl. Acad. Sci. USA</u> 85:8855-8859 (1988)	

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X	A48	MOSMANN, "Rapid Colorimetric Assay for Cellular Growth and Survival: Application to Proliferation and Cytotoxicity Assays," <u>J. Immunol. Methods</u> 65:55-63 (1983) © Elsevier Publishers B.V.	
X	A49	PLOWMAN et al., "Receptor Tyrosine Kinases as Targets for Drug Intervention," <u>DN&amp;P</u> 7:334-339 (1994)	
X	A50	RYGAARD and POVLSEN, "Heterotransplantation of a Human Malignant Tumour to 'Nude' Mice," <u>Acta Path. Microbiol. Scand.</u> 77:758-760 (1969)	
X	A51	SANDBERG-NORDQUIST et al., "Characterization of Insulin-Like Growth Factor 1 in Human Primary Brain Tumors," <u>Cancer Research</u> , 53:2475-2478, (1993)	
X	A52	SCHLESSINGER and ULLRICH, "Growth Factor Signalling by Receptor Tyrosine Kinases," <u>Neuron</u> , 9:383-391, (1992)	
X	A53	SLAMON et al., "Studied of the HER-2/ <i>neu</i> Proto-oncogene in Human Breast and Ovarian Cancer," <u>Science</u> , 244:707-712, (1989)	
X	A54	SONGYANG et al. "Specific Motifs Recognized by the SH2 Domains of Csk 3BP2, fps/fes, GRB-2, HCP, SHC, Syk and Vav," <u>Molecular and Cellular Biology</u> , 14:2777-2785 (1994)	
X	A55	SONGYANG et al., "SH2 Domains Recognize Specific Phosphopeptide Sequences," <u>Cell</u> 72:767-778 (1993)	
<	A56	SUPERTI-FURGA et al., "A functional screen in yeast for regulators and antagonizers of heterologous protein tyrosine kinsases," <u>Nature Biotech</u> 14:600-605 (1996)	
X	A57	SUPERTI-FURGA et al., "Csk inhibition of c-Src activity requires both the SH2 and SHS domains of Src," <u>EMBO J.</u> , 12:2625-2634 (1993)	
X	A58	TAKANO et al., "Inhibition of angiogenesis by a novel diaminoanthraquinone that inhibits protein kinase C," <u>Mol. Bio. Cell</u> , 4:358A at abstract no. 2076 (1993)	
X	A59	TORP et al., "Expression of the Epidermal Growth Factor Receptor Gene in Human Brain Metastases," <u>AMPIS</u> , 100:713-719 (1992)	

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X	A60	TUZI et al., "Expression of growth factor receptors in human brain tumours," <u>Br. J. Cancer</u> , 63:227-233 (1991)	
X	A61	VENUGOPALAN et al., STN International® CAPLUS Database, Accession No. 1990:459109, <u>Indian J. Chem.</u> , 29B(4), 364-365, (1990)	
X	A62	VENUGOPALAN et al., STN International® CAPLUS Database, Accession No. 1990:23849, <u>Eur. J. Med. Chem.</u> , 24(6), 611-614, (1989)	
X	A63	VENUGOPALAN et al., STN International® CAPLUS Database, Accession No. 1993:517279, Indian Patent Application IN 167426, published 27 October 1990	
X	A64	VOLLER et al., "Ch. 45 - Enzyme-Linked Immunosorbent Assay," in <u>Manual of Clinical Immunology</u> , 2 <sup>nd</sup> edition, Rose and Friedman editors, American Society of Microbiology, Washington, D.C., pp. 359-371, (1980)	
X	A65	WAKABAYASHI et al., STN International® CAPLUS Database, Accession No. 1995:839583, <u>Proceedings of the International Symposium of the Princess Takamatsu Cancer Research Fund</u> , 1995 (abstract)	
X	A66	WRIGHT et al., "Inhibition of Angiogenesis in Vitro and In Ovo with an Inhibitor of Cellular Protein Kinases, MDL 27032," <u>J. Cellular Physiology</u> , 152:448-457 (1992)	

X Did not receive

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